"On the Physical Relation of Chloroform to Blood." By A. D. Waller, M.D., F.R.S. Received May 5,—Read June 9, 1904.

In connection with the preliminary communication by Moore and Roaf on certain physical and chemical properties of solutions of chloroform in water, saline, serum, and hæmoglobin,* it may be of interest to publish the following communication. The close similarity of the conclusions arrived at independently by different observers is such as to render the two communications mutually corroborative, and although the present communication forms part of a report by A. D. Waller and J. H. Wells, which is technically the property of a Special Chloroform Committee of the British Medical Association, there is obviously no reason why it should be withheld from publication. It was originally presented as long ago as June 19, 1903, and I have since that time extended the experimental data upon which the conclusion rests. In order, however, to preserve the complete independence of the two contributions I have preferred to communicate it in its original, and perhaps imperfect, form. The importance of the blood as a chloroform carrier, by reason, presumably, of an easily dissociable compound, is the conclusion of principal importance arrived at in both series of investigations.

The original text of the report is as follows :—

"Our attempts to recover a known weight of chloroform from blood, by the French method (extraction *in vacuo* followed by digestion with alcoholic potash and titration of chlorides), led us to make two simple experiments that very strikingly illustrate the fundamental difference between blood and simple salt solution or water as regards their absorptive power towards chloroform vapour. The first of these experiments shows that equal volumes of blood and of normal saline are capable of absorbing very different volumes of chloroform vapour. The second shows the converse fact that very different volumes of chloroform vapour are obtainable by evacuating equal volumes of blood and of water, or of normal saline. In the first experiment the absorption by blood is greater than that by water. In the second experiment the delivery from blood is less than that from water. The inference from these two data is that blood possesses greater affinity for chloroform than does water, and that, therefore, in the transfer of chloroform by blood from the pulmonary air to the nervous centres that fluid does not act as a simple solvent, but rather as a temporary retaining and restraining medium, that helps to convert irregular into constant flow. The blood has thus a controlling effect upon the process of anæsthesia that may be compared to the action of a fly-

* Communicated by Professor Sherrington, received April 12, read May 5, 1904. [*Ante*, pp. 382—412.]

wheel, or to that of the arterial elasticity, by which intermittent force effects constant flow. The blood acts as a chloroform reservoir (or as an ether reservoir if ether be the anæsthetic employed).

In the *first experiment* we compared manometrically the absorptive power of blood and of water by introducing a known volume of each liquid in the two identical closed flasks connected with two petroleum manometers, and previously filled with chloroform and air of identical percentage.

The figures of a first trial were as follows for 50 c.c. of blood* and of water respectively in flasks of 600 c.c. capacity filled with chloroform vapour at 17 per cent. :—

| Time of absorption. | Flask A. Water-absorption pressure. | Flask B. Blood-absorption pressure. |
|---|---|---|
| 1 min. | 186 mm. | 243 mm. |
| 20 mins. | 191 | 246 |
| 60 | 192 | 246 |

A second trial, with the blood and water transposed, and the flasks charged by chloroform and air at lower $CHCl_3$ percentages gave :—

| $CHCl_3$ in flask. | Time of absorption. | Flask A. Blood-absorption pressure. | Flask B. Water-absorption pressure. |
|---|---|---|---|
| 10 per cent. | 4 mins. | 110 mm. | 56 mm. |
| | 7 | 140 | 82 |
| | 12 | 156 | 88 |
| | 16 | 167 | 90 |
| | 21 | 170·5 | 92 |
| 6 „ | 0 | 35 | 34 |
| | 4 | 62·5 | 43 |
| | 9 | 69 | 44 |
| | 13 | 71 | 45 |
| | 17 | 72 | 50 |
| | 60 | 75 | 54 |

* The blood in this experiment was taken from the chloroformed animal, *i.e.*, contained *some* chloroform. Blood fully saturated with chloroform has no further absorptive power. Blood from an unchloroformed animal has a maximum absorptive power. We have made preliminary trials to learn whether a rapid method of estimating the degree of saturation of blood with chloroform can be based on this principle, but our results at present are not sufficiently advanced for report. The figures given in the text are preliminary approximations, obtained by a first trial of a method which will require much further elaboration as regards its apparatus. It will be noticed that the gross difference in favour of blood comes out in spite of the fact that the water value and solvent power of blood are about 0·8 that of water.

The first part of the absorption is lost in each case during introduction of fluid into the bottles. The first pair of readings are taken at the end of the second minute. The second readings at the end of the fourth minute, when both bottles are equally shaken for half a minute, after which the third readings are taken. The fourth and fifth readings are similarly taken at the seventh minute, the bottles being shaken a second time, $S_2$.

The bottles are left at rest for 7 minutes before the last readings, which show that the absorption has been nearly but not quite completed.

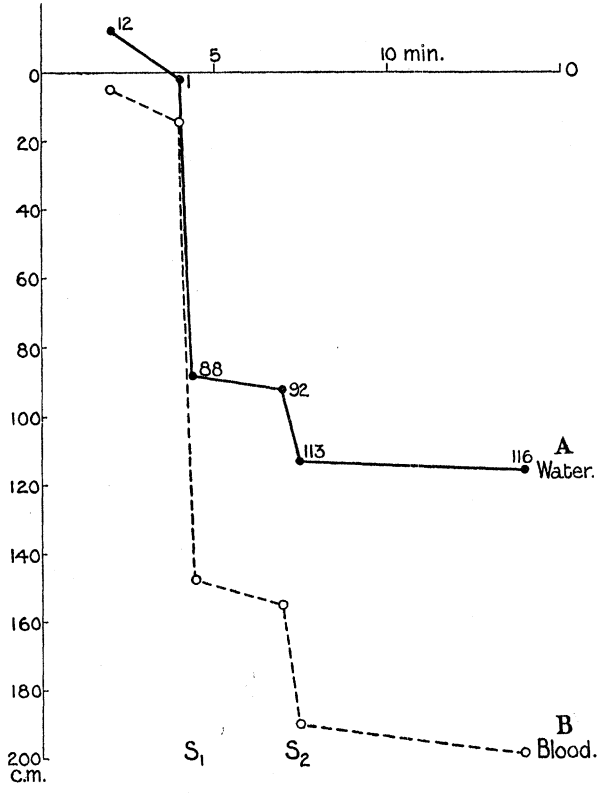


Figure showing Absorption Curves of Chloroform Vapour by Water and by Blood.

The vapour in the two bottles was then passed into and through two densimeter bulbs by water displacement. The increments of weight in the two cases were: in A 0·054 gramme, in B 0·032 gramme, showing that the residual atmosphere in A (water) contained more chloroform vapour than that in B (blood).

In the *second experiment* the apparatus consisted of (1) a distilling flask (containing the fluid to be evacuated, and a known weight of chloroform in a small glass bulb), (2) a receiver, and (3) a Geryk air-pump.

The receiver is first evacuated while shut off from the distiller. It is then shut off from the pump, and placed in connection with the distilling flask, with the result that the liquid in the latter boils and gives up its dissolved gases, which are for the most part drawn over into the receiver.

The evacuation of $CHCl_3$ is completed (in the case of saline; it is not completed in the case of blood) by gentle heat, and by opening the inlet of the distilling flask so that a rush of air takes place through the distiller to the receiver. The inlet tube is drawn out to a fine point, and reaches to the bottom of the distilling flask; the outlet tube is provided with a froth-bulb. Finally the quantity of $CHCl_3$ in the receiver is estimated by Harcourt's method.

In a *first trial* of this experiment with water in the distilling flask the result was as follows :—

| | |
|---|---|
| Weight of $CHCl_3$ taken ..... | 0·082 gramme |
| „ recovered..... | 0·065 „ |
| Deficit..... | 0·017 „ |
| | or 21 per 100. |

This considerable deficit was attributable to an insufficient capacity of the receiver as compared with that of the distiller and froth-bulb. That this was the case is shown by the figures of a second trial, in which a larger receiver was taken (of 1332 c.c. capacity in place of 400 c.c. capacity in the previous trial).

In this *second trial* the figures came out :—

| | |
|---|---|
| Weight of $CHCl_3$ taken ..... | 0·112 gramme |
| „ recovered..... | 0·109 „ |
| Deficit..... | 0·003 „ |
| | or 3 per 100. |

The similar experiment, with blood in place of water, gave a very different result, the deficit of evacuation being much greater, and clearly signifying that the chloroform is not merely in solution, but held in combination. In a carefully conducted trial made with 50 c.c. of whipped bullock's blood, to which 0·108 gramme of $CHCl_3$ had been added, the weight recovered was only 0·014 gramme; *i.e.*, the deficit was 0·092 gramme, or 85 per cent. It is evident, therefrom, that the absorption of chloroform by blood does not follow Henry's law.

This conclusion is in agreement with that arrived at by previous observers, Hermann, Schmiedeberg and others, to the effect that chloroform combines with the lecithin of blood. It is also in harmony with the modern theory of anæsthesia as presented by recent writers (H. Mayer, Overton, H. Meyer)* to the effect that the action of anæsthetics upon the several tissues and fluids of the body depends upon a "coefficient of partage, in which the affinity between anæsthetic and fatty matter is the principally effective factor."

From the foregoing observations (which should properly have been published by the Special Chloroform Committee in July of last year) it is clear that the conclusions are substantially identical with that arrived at by Moore and Roaf, viz., that the absorption of chloroform vapour is greater by blood than by saline, and that blood acts as chloroform carrier to the tissues just as it acts as oxygen carrier. It is a minor point of difference between the two independently presented conclusions, that whereas Moore and Roaf find no proof of any special combination between chloroform and "lipoids" as previously urged by German observers, we have in the report of our experiments admitted that the combination which certainly takes place between chloroform and protoplasm may possibly be accounted for on the lipoid theory.

But the question whether chloroform can combine with all protoplasm indifferently, or with its fatty constituents (lecithin, cholesterin) more particularly is a subsidiary issue, in respect of which neither the observations of Moore and Roaf, nor our own, contain any decisive evidence. On the one hand we are in presence of the fact that all protoplasm is subject to the influence of chloroform, on the other with the fact that all protoplasm is associated with fatty constituents of which lecithin is the most universal representative. Lecithin is widely distributed in vegetable as well as in animal protoplasm; it is present in blood-serum, which, as shown by Moore and Roaf, has a solvent power towards chloroform not far short of that possessed by blood.

* Schmiedeberg, 'Grundriss der Pharmakologie'; Overton, 'Pflüger's Archiv'; H. Meyer, 'Arch. f. exp. Path. u. Pharm., vol. 42, p. 109, 1899; Höber, 'Physikalische Chemie'; Gottlieb, 'Ergebnisse der Physiologie,' "Theorie de Narkose," vol. 2, p. 666, 1902.